

# Temporal Differentiation and the Optimization of System Output

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This paper develops a set of simplified dynamical models with which to explore the conditions under which temporal differentiation leads to optimized system output. By temporal differentiation, we mean a division of labor whereby different subtasks associated with performing a given task are done at different times. The idea is that, by focusing on one particular set of subtasks at a time, it is possible to increase the efficiency with which each subtask is performed, thereby allowing for faster completion of the overall task. For this paper, we consider a process whereby some resource is converted into some final product in a series of three agent-mediated steps. Temporal differentiation is incorporated by allowing the agents to oscillate between performing the first two steps and performing the last step. We find that temporal differentiation is favored when the number of agents is small, and when the process intermediates have a much longer lifetime than the original resource. Within the framework of biological systems, we argue that these results provide a possible evolutionary basis for the emergence of sleep, and also of distinct REM and non-REM sleep states. We also discuss our use of a three-step model. Briefly, in order for temporal differentiation to increase product output in a mean-field description of resource metabolism, it is necessary for temporal differentiation to have a nonlinear effect on individual process rates. For stochastic models, we argue that temporal differentiation can increase product output even in fundamentally linear systems.

Keywords: Temporal differentiation, division of labor, REM and non-REM sleep, agent-based models

## I. INTRODUCTION

Differentiation and the division of labor is a ubiquitous phenomenon characterizing the emergence of complex systems. Different enzymes, nucleic acids and other biopolymers are involved in the proper function of a living cells. In multicellular organisms, cells differentiate and specialize in the performance of one or a few tasks. At higher levels of complexity, multicellular organisms, e.g. humans, can themselves form highly differentiated structures (a modern networked economy), where each organism performs one or a few tasks [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13].

As a result of the ubiquity of the division of labor in biology, considerable experimental and theoretical work has been devoted to understanding both its genetic basis, and the selection pressures that give rise to such behaviors. In a general sense, division of labor is favored when transport costs associated with delivering process intermediates to the appropriate agents are small. Therefore, division of labor is generally favored at high population densities, though this may not always be the case [10, 14].

In this paper, we wish to discuss another form of differentiation, specifically *temporal differentiation*. Temporal differentiation refers to a division of labor where a given task is broken up into several subtasks, and the various subtasks are performed at different times. That is, with temporal differentiation, a given set of agents performs all the subtasks associated with a given task. However, these agents concentrate their efforts on one set of subtasks for a certain period of time, and then concentrate

their efforts on another set of subtasks for another period of time. This is in contrast to the “standard” picture of division of labor, whereby all subtasks associated with a given task are performed simultaneously by different sets of agents.

Temporal differentiation, although a perhaps less obvious form of division of labor, is nevertheless also a ubiquitous phenomenon. At the level of task completion by humans, it is quite common that various tasks are often done in intermittent blocs. Examples include paying of bills, housekeeping chores, and the procurement of food. Such forms of temporal differentiation are likely prevalent in other organisms, since such a temporally differentiated labor strategy is a natural approach in many contexts for optimizing system efficiency.

Another, more subtle form of temporal differentiation is the phenomenon of sleep. Sleep is prevalent in organisms with highly complex central nervous systems. It is characterized by periods of high levels of alertness, followed by periods during which the brain goes into an unconscious state.

One theory, due to Crick and Mitchison, for the existence of sleep, is that sleep is a time when the brain engages in various garbage collection activities [15]. More specifically, sleep is a time when the brain sorts through and consolidates information accumulated from the previous period of wakefulness [16, 17, 18, 19, 20, 21]. Increasing evidence suggests that Crick and Mitchison’s basic hypothesis may be correct [22]. Nevertheless, while this “garbage collection” hypothesis provides an explanation for what happens during sleep, it does not explain the selection pressures driving the emergence of this phenomenon.

In two recent papers [23, 24], the author suggested that sleep emerges because, in the presence of a day-night cy-

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cle, it is optimal for a highly complex brain to engage in information collection activities during the day, when light information is most available, and then to engage in information consolidation (i.e. “garbage collection”) activities at night, when light information is far less available. The idea is that, by concentrating on information collection when it is available, and information consolidation when external information is less available, the brain can process an optimal amount of information in a given amount of time, which presumably confers a survival advantage to the organism.

However, such an explanation is incomplete, since some organisms are nocturnal. Further, what is interesting about the sleep state itself is that it is divided into distinct, alternating cycles of REM and non-REM sleep (where REM stands for “Rapid Eye Movement”) [15, 16, 25]. However, not all sleeping organisms exhibit REM and non-REM sleep. In particular, the organism *Tachyglossus aculeatus*, a representative of the earliest branch of mammalian evolution (the monotremes), combines both REM and non-REM sleep into one sleep state [26]. This suggests that REM and non-REM sleep are not fundamental to sleep itself, but rather emerged via the differentiation of a single, older sleep state.

Therefore, it is possible that temporal differentiation of various brain tasks leads to optimized brain function in higher organisms, independent of any external day-night regulation cycle. The existence of a day-night cycle simply regulates the optimal start times for each task period. Furthermore, it is also possible that temporal differentiation is favored the more work needs to be completed within a given time period. In the context of REM and non-REM sleep, it is possible that mammals with simpler brains can perform the information consolidation tasks in one sleep state. However, for larger, more complex mammalian brains, the amount of information consolidation to be performed becomes sufficiently large that it becomes more efficient to divide the various information consolidation subtasks into two distinct sleep states.

Motivated by these various considerations, we present a highly simplified model for the processing of some resource into a final product. The processing of this resource occurs in three separate steps, each mediated by an agent. Because our model adopts the notation and structure of the theory of chemical reaction kinetics, the various agents involved in each subtask are represented as enzyme catalysts.

When there is no temporal differentiation, all three subtasks are performed simultaneously, and the fraction of enzymes assigned to each task is constant in time. With temporal differentiation in the context of our model, the enzymes oscillate between performing the first two tasks for a certain amount of time, and then the third task for another amount of time. We use a three-subtask model because, in the mean-field approach that we adopt here, a minimum of three subtasks is necessary in order to achieve the nonlinear dependence of task rate on enzyme number required to give an advantage to a

temporally differentiated labor strategy. For stochastic models, this fundamentally nonlinear dependence of task rate on enzyme number is not necessary, an issue which we will discuss later.

Within the framework of our model, we find that temporal differentiation is favored when the amount of available agents is at intermediate values compared to the rate of resource input, and when the intermediate products have a long lifetime compared to the starting resource. It therefore makes sense to focus entirely on one set of tasks for a time, to convert as much resource as possible into a long-lived intermediate, and then switch to processing the intermediate.

This paper is organized as follows: In the following section (Section II), we develop our three-process model, and derive the limiting form of the model when the total number of enzymes is small. In Section III, we go on to solve our model with and without temporal differentiation. In Section IV, we compare both the temporally differentiated and non-differentiated strategies, and determine the regimes where one strategy is expected to be favored over the other. In Section V we discuss our results in the context of sleep and other examples of temporal differentiation in biology. Finally, in Section VI we present our main conclusions. We also describe some shortcomings of our model, and how our model may be further developed in future work.

## II. THE MODEL

In this section, we introduce our three process model, whereby an external resource is converted into a final product in a series of three steps. We set up dynamical equations governing the production of final product for both the temporally differentiated and non-differentiated cases.

### A. Definition of the model

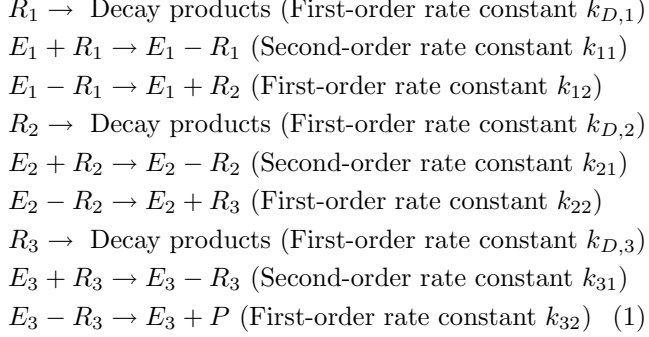
Our model consists of some compartment of fixed volume  $V$ , into which flows a resource, denoted  $R_1$ , at some fixed rate  $f_R$ . This resource is processed into a final product, denoted  $P$ , via a series of three agent-mediated, or, in the language of chemical kinetics, enzyme-catalyzed, steps.

In the first step, an enzyme, denoted  $E_1$ , binds to  $R_1$ , and then converts  $R_1$  into an intermediate  $R_2$ . In the second step, an enzyme, denoted  $E_2$ , binds to  $R_2$ , and then converts  $R_2$  into an intermediate  $R_3$ . In the third and final step, an enzyme, denoted  $E_3$ , binds to  $R_3$ , and then converts  $R_3$  into the final product  $P$ .

Furthermore, the resource  $R_1$  and intermediates  $R_2$ ,  $R_3$  have finite lifetimes in the compartment, defined by first-order decay constants  $k_{D,1}$ ,  $k_{D,2}$ , and  $k_{D,3}$ , respectively. These decay terms can be due to various factors, such as diffusion out of the compartment, or simply

the physical decay of the components themselves. In the context of networked systems and data processing, these decay constants can also correspond to a finite lifetime during which an information packet is relevant (say stock information that is used by an investor to decide whether or not to invest in a given stock).

In the language of chemical kinetics, the set of reactions in the compartment is given by,



Letting  $n_{R_i}$  denote the number of particles of resource  $R_i$ ,  $n_{E_i}$  the number of particles of enzyme  $E_i$ , and  $n_{E_i R_i}$  the number of particles of  $E_i - R_i$ , where  $i = 1, 2, 3$ , we obtain the following system of differential equations for the time evolution of the numbers of the various components in the compartment:

$$\begin{aligned}
\frac{dn_{R_1}}{dt} &= f_R - \frac{k_{11}}{V} n_{E_1} n_{R_1} - k_{D,1} n_{R_1} \\
\frac{dn_{E_1 R_1}}{dt} &= \frac{k_{11}}{V} n_{E_1} n_{R_1} - k_{12} n_{E_1 R_1} \\
\frac{dn_{R_2}}{dt} &= k_{12} n_{E_1 R_1} - \frac{k_{21}}{V} n_{E_2} n_{R_2} - k_{D,2} n_{R_2} \\
\frac{dn_{E_2 R_2}}{dt} &= \frac{k_{21}}{V} n_{E_2} n_{R_2} - k_{22} n_{E_2 R_2} \\
\frac{dn_{R_3}}{dt} &= k_{22} n_{E_2 R_2} - \frac{k_{31}}{V} n_{E_3} n_{R_3} - k_{D,3} n_{R_3} \\
\frac{dn_{E_3 R_3}}{dt} &= \frac{k_{31}}{V} n_{E_3} n_{R_3} - k_{32} n_{E_3 R_3} \quad (2)
\end{aligned}$$

We also define the quantities  $n_1$ ,  $n_2$ , and  $n_3$  via,

$$\begin{aligned}
n_1 &= n_{E_1} + n_{E_1 R_1} \\
n_2 &= n_{E_2} + n_{E_2 R_2} \\
n_3 &= n_{E_3} + n_{E_3 R_3} \quad (3)
\end{aligned}$$

so that  $n_1$ ,  $n_2$ , and  $n_3$  denote the total amount of  $E_1$ ,  $E_2$ , and  $E_3$  respectively at some given time.

Note that our model is essentially a mean-field description of the dynamics inside the compartment, since we are assuming that the amount of each component can take on any nonnegative real number.

### B. Temporal differentiation in the three-enzyme compartment model

Temporal differentiation can occur in our model if we do not assume that  $n_1$ ,  $n_2$ , and  $n_3$  are fixed, but rather

can oscillate in time. For the purposes of this paper, we will assume that  $n_1$ ,  $n_2$ , and  $n_3$  oscillate in such a way that  $n_1 = n_1^+$ ,  $n_2 = n_2^+$ , and  $n_3 = n_3^-$  over some time period of length  $T_1$ , followed by a time period of length  $T_2$  where  $n_1 = n_1^- \leq n_1^+$ ,  $n_2 = n_2^- \leq n_2^+$ , and  $n_3 = n_3^+ \geq n_3^-$ . We assume that the total number of enzymes remains fixed, however, so that  $n_1^+ + n_2^+ + n_3^- = n_1^- + n_2^- + n_3^+$ .

Essentially, if we switch from an enzyme-based viewpoint to an agent-based viewpoint, our model assumes that agents can switch from one set of tasks to another. In this model, the agents alternate between focusing on the first two processes and the third process. In the chemical kinetics notation, we have,



For the purposes of this paper, we will assume that the rate constant of this “task-switching” reaction is  $\infty$ . Therefore, each agent can instantaneously switch from one task to another, if it so chooses. Toward the end of this paper we will speculate on the effect that a finite task-switching rate has on the results presented here.

### C. Limiting forms of the model

We will now study how our model behaves when  $n_1 + n_2 + n_3$  and  $k_{D,3}$  may each be regarded as “small” in some sense. The criterion for smallness will be defined later, once we have established the behavior of the model in these regimes.

To begin, we note from the previous subsection that the various enzyme numbers fluctuate in time. More precisely, there exist  $T_1, T_2 > 0$  such that for every integer  $s$ , the total enzyme numbers for each enzyme are at  $n_1^+$ ,  $n_2^+$ ,  $n_3^-$  respectively, during the time interval  $[s(T_1 + T_2), s(T_1 + T_2) + T_1]$ , while during the time interval  $[s(T_1 + T_2) + T_1, (s + 1)(T_1 + T_2)]$ , the enzyme numbers are at  $n_1^-$ ,  $n_2^-$ , and  $n_3^+$ .

If we define,

$$\bar{n}_{1/2/3} = \frac{n_{1/2/3}^+ + n_{1/2/3}^-}{2} \quad (5)$$

and,

$$\lambda_{1/2/3} = \frac{n_{1/2/3}^+ - n_{1/2/3}^-}{n_{1/2/3}^+ + n_{1/2/3}^-} \quad (6)$$

then it may be readily shown that,

$$n_{1/2/3}^\pm = \bar{n}_{1/2/3} (1 \pm \lambda_{1/2/3}) \quad (7)$$

For fixed values of  $\lambda_1$ ,  $\lambda_2$ , we wish to develop a form for the first four equations assuming that  $\bar{n}_1$ ,  $\bar{n}_2$  are small. The overall strategy is as follows: Because  $R_3$  is the intermediate that feeds into the third task, our goal is to determine the rate of production of  $R_3$  when  $\bar{n}_1$ ,  $\bar{n}_2$  are

small. By this we mean that we seek to determine, with respect to  $\bar{n}_1$  and  $\bar{n}_2$ , the lowest-order term contributing to the production rate of  $R_3$ .

When  $\bar{n}_1 = 0$ , we have that  $n_{E_1 R_1} = n_{E_1} = n_{R_2} = n_{E_2 R_2} = n_{E_2} = 0$ . If we let  $n_{R_1,0}$  denote  $n_{R_1}$  when  $\bar{n}_1 = 0$ , we obtain,

$$\frac{dn_{R_1,0}}{dt} = f_R - k_{D,1}n_{R_1,0} \quad (8)$$

Differentiating the second equation with respect to  $\bar{n}_1$ , and setting  $n_{E_1 R_1,1} = (\partial n_{E_1 R_1} / \partial \bar{n}_1)_{\bar{n}_1=0}$ , we obtain,

$$\frac{dn_{E_1 R_1,1}}{dt} = \frac{k_{11}}{V}(1 \pm \lambda_1)n_{R_1,0} - \left(\frac{k_{11}}{V}n_{R_1,0} + k_{12}\right)n_{E_1 R_1,1} \quad (9)$$

Differentiating the third equation with respect to  $\bar{n}_1$ , and setting  $n_{R_2,1} = (\partial n_{R_2} / \partial \bar{n}_1)_{\bar{n}_1=\bar{n}_2=0}$ , we obtain,

$$\frac{dn_{R_2,1}}{dt} = k_{12}n_{E_1 R_1,1} - k_{D,2}n_{R_2,1} \quad (10)$$

Note that  $n_{E_2} = n_{E_2 R_2} = 0$  when  $\bar{n}_2 = 0$ . Therefore, derivatives of these quantities that only involve  $\bar{n}_1$  will be 0 when evaluated at  $(\bar{n}_1, \bar{n}_2) = (0, 0)$ . So, the lowest-order derivative at  $n_{E_2 R_2}$  that is possibly non-vanishing at  $(\bar{n}_1, \bar{n}_2) = (0, 0)$  is  $\partial^2 n_{E_2 R_2} / (\partial \bar{n}_1 \partial \bar{n}_2)$ . Defining  $n_{E_2 R_2,1} = (\partial^2 n_{E_2 R_2} / (\partial \bar{n}_1 \partial \bar{n}_2))_{(\bar{n}_1, \bar{n}_2)=(0,0)}$ , we obtain,

$$\frac{dn_{E_2 R_2,1}}{dt} = \frac{k_{21}}{V}(1 \pm \lambda_2)n_{R_2,1} - k_{22}n_{E_2 R_2,1} \quad (11)$$

Note that the lowest order term contributing to the production rate of  $R_3$  is given by  $n_{E_2 R_2,1}\bar{n}_1\bar{n}_2$ .

For the first four equations, we obtain the linearized system,

$$\begin{aligned} \frac{dn_{R_1,0}}{dt} &= f_R - k_{D,1}n_{R_1,0} \\ \frac{dn_{E_1 R_1,1}}{dt} &= \frac{k_{11}}{V}(1 \pm \lambda_1)n_{R_1,0} - \left(\frac{k_{11}}{V}n_{R_1,0} + k_{12}\right)n_{E_1 R_1,1} \\ \frac{dn_{R_2,1}}{dt} &= k_{12}n_{E_1 R_1,1} - k_{D,2}n_{R_2,1} \\ \frac{dn_{E_2 R_2,1}}{dt} &= \frac{k_{21}}{V}(1 \pm \lambda_2)n_{R_2,1} - k_{22}n_{E_2 R_2,1} \end{aligned} \quad (12)$$

For the final two equations, we assume that  $k_{D,3} = 0$ , giving,

$$\begin{aligned} \frac{dn_{R_3}}{dt} &= k_{22}n_{E_2 R_2} - \frac{k_{31}}{V}n_{E_3}n_{R_3} \\ \frac{dn_{E_3 R_3}}{dt} &= \frac{k_{31}}{V}n_{E_3}n_{R_3} - k_{32}n_{E_3 R_3} \end{aligned} \quad (13)$$

We will discuss the assumption of  $k_{D,3} = 0$  later in this paper.

### III. LONG TIME BEHAVIOR OF THE MODEL

In the absence of temporal differentiation, the values of  $n_1, n_2, n_3$  remain constant, and so we expect the dynamics to evolve to a steady-state. With temporal differentiation, the values of  $n_1, n_2, n_3$  oscillate between two sets of values over a well-defined time period  $T_1 + T_2$ . Therefore, in this situation, we cannot expect the dynamics to settle into a steady-state solution. However, we can expect the dynamics to settle into a periodic solution.

In this section, we therefore consider the long-term behavior of our model with and without temporal differentiation. Without temporal differentiation, that is, assuming that  $\lambda_1 = \lambda_2 = \lambda_3 = 0$ , we look for steady-state solutions to the dynamical system. With temporal differentiation, we look for periodic solutions to the dynamical system. We will consider the case where  $\lambda_1 = \lambda_2 = \lambda_3 = 1$ . Here, the enzymes devote themselves entirely to the first two tasks over a time interval of length  $T_1$ , and then devote themselves to the third task over a time interval of length  $T_2$ .

#### A. Case 1: $\lambda_1 = \lambda_2 = \lambda_3 = 0$

When  $\lambda_1 = \lambda_2 = \lambda_3 = 0$ , there is no fluctuation in the total enzyme numbers for either  $E_1, E_2$ , or  $E_3$ . Therefore, the long-time solution is simply a steady-state solution. Setting the left-hand sides of the four linearized equations to 0 gives,

$$\begin{aligned} n_{R_1,0} &= \frac{f_R}{k_{D,1}} \\ n_{E_1 R_1,1} &= \frac{\frac{f_R}{k_{12}}}{\frac{f_R}{k_{12}} + \frac{k_{D,1}}{(k_{11}/V)}} \\ n_{R_2,1} &= \frac{k_{12}}{k_{D,2}} \frac{\frac{f_R}{k_{12}}}{\frac{f_R}{k_{12}} + \frac{k_{D,1}}{(k_{11}/V)}} \\ n_{E_2 R_2,1} &= \frac{(k_{21}/V)}{k_{D,2}} \frac{k_{12}}{k_{22}} \frac{\frac{f_R}{k_{12}}}{\frac{f_R}{k_{12}} + \frac{k_{D,1}}{(k_{11}/V)}} \end{aligned} \quad (14)$$

If we define  $A$  and  $B$  via,

$$\begin{aligned} A &= \frac{(k_{11}/V)}{k_{D,1}} f_R \\ B &= \frac{(k_{11}/V)}{k_{D,1}} f_R + k_{12} \end{aligned} \quad (15)$$

then we obtain that the rate of production of  $R_3$  is  $k_{12}(k_{21}/V)/k_{D,2}(A/B)\bar{n}_1\bar{n}_2$ .

Now, the maximal production rate of  $P$  is obtained when  $n_{R_3} = \infty$ . The reason for this is that the rate of the third binding step is then infinite, so that the production rate of  $P$  is only limited by the rate at which the enzyme  $E_3$  can convert  $R_3$  into  $P$ .

When  $n_{R_3} = \infty$ , the rate of production of  $P$  is given by  $k_{32}n_{E_3R_3} = k_{32}\bar{n}_3$ . At steady-state, the rate of production of  $R_3$  must equal the rate of production of  $P$  (since the production rate of  $P$  is equal to the consumption rate of  $R_3$  when  $k_{D,3} = 0$ ). Therefore, at steady-state,

$$k_{12}\frac{(k_{21}/V)}{k_{D,2}}\left(\frac{A}{B}\right)\bar{n}_1\bar{n}_2 = k_{32}\bar{n}_3 \quad (16)$$

Now, defining  $n = \bar{n}_1 + \bar{n}_2 + \bar{n}_3$ ,  $\alpha = (\bar{n}_1 + \bar{n}_2)/n$ ,  $\beta = \bar{n}_1/(\bar{n}_1 + \bar{n}_2)$ , we have, at steady-state,

$$\frac{dn_P}{dt} = k_{12}\frac{(k_{21}/V)}{k_{D,2}}\left(\frac{A}{B}\right)\alpha^2\beta(1-\beta)n^2 = k_{32}(1-\alpha)n \quad (17)$$

Therefore, the steady-state production rate of  $P$  is maximized when  $\beta = 1/2$ , and so we wish to solve,

$$\alpha^2 + \frac{1}{\gamma n}\alpha - \frac{1}{\gamma n} = 0 \quad (18)$$

where,

$$\gamma \equiv \frac{k_{12}\frac{(k_{21}/V)}{k_{D,2}}\left(\frac{A}{B}\right)}{4k_{32}} \quad (19)$$

This gives,

$$\alpha = \frac{1}{2}\frac{1}{\gamma n}[-1 + \sqrt{1 + 4\gamma n}] \Rightarrow 1 - \alpha = \frac{1 + 2\gamma n - \sqrt{1 + 4\gamma n}}{2\gamma n} \quad (20)$$

The steady-state production rate of  $P$  is then given by  $k_{32}(1 - \alpha)n$ . To distinguish this value of  $\alpha$  from the value of  $\alpha$  we will obtain in the temporally differentiated model, we re-denote the  $\alpha$  here  $\alpha_{undiff}$ .

## B. Case 2: $\lambda_1 = \lambda_2 = \lambda_3 = 1$

When  $\lambda_1 = \lambda_2 = \lambda_3 = 1$ , then the enzyme levels for enzymes  $E_1$  and  $E_2$  are at their maximal levels during the time interval  $[s(T_1 + T_2), s(T_1 + T_2) + T_1]$ , and are not present during the time interval  $[s(T_1 + T_2) + T_1, (s + 1)(T_1 + T_2)]$ . Therefore, in the time interval  $[s(T_1 + T_2) + T_1, (s + 1)(T_1 + T_2)]$ , we have  $n_{E_1} = n_{E_1R_1} = n_{E_2} = n_{E_2R_2} = 0$ .

By periodicity and continuity it follows that, in the time interval  $[s(T_1 + T_2), s(T_1 + T_2) + T_1]$ , we have the initial conditions  $n_{E_1} = 2\bar{n}_1$ ,  $n_{E_1R_1} = 0$ ,  $n_{E_2} = 2\bar{n}_2$ ,  $n_{E_2R_2} = 0$ . Starting with these initial conditions, we have that the solution to the differential equation for  $n_{R_1,0}$  is,

$$n_{R_1,0}(\Delta t) = n_{R_1,0}(0)e^{-k_{D,1}\Delta t} + \frac{f_R}{k_{D,1}}(1 - e^{-k_{D,1}\Delta t}) \quad (21)$$

where  $\Delta t = t - s(T_1 + T_2)$ .

The periodicity condition means that we want  $n_{R_1,0}(T_1 + T_2) = n_{R_1,0}(0)$ , giving  $n_{R_1,0}(0) = f_R/k_{D,1}$ , which then implies that  $n_{R_1,0}(\Delta t) = f_R/k_{D,1}$  for all  $\Delta t$ .

So for  $R_1$ , the lowest-order nonvanishing term for  $n_{R_1}$  is unaffected by a temporal division of labor.

Turning to  $n_{E_1R_1,1}$ , we have, in the time interval  $[s(T_1 + T_2), s(T_1 + T_2) + T_1]$ , the differential equation,

$$\frac{dn_{E_1R_1,1}}{dt} = 2\frac{k_{11}}{V}\frac{f_R}{k_{D,1}} - \left(\frac{k_{11}}{V}\frac{f_R}{k_{D,1}} + k_{12}\right)n_{E_1R_1,1} \quad (22)$$

which may be solved to give,

$$n_{E_1R_1,1}(\Delta t) = 2\frac{A}{B}(1 - e^{-B\Delta t}) \quad (23)$$

where  $A$  and  $B$  were defined in the previous subsection.

The differential equation for  $n_{R_2,1}$  takes on two distinct forms, depending on the time interval we are in. For  $t \in [s(T_1 + T_2), s(T_1 + T_2) + T_1]$ ,  $[s(T_1 + T_2) + T_1, (s + 1)(T_1 + T_2)]$ , the differential equations are, respectively,

$$\begin{aligned} \frac{dn_{R_2,1}}{dt} &= 2k_{12}\frac{A}{B} - 2k_{12}\frac{A}{B}e^{-B\Delta t} - k_{D,2}n_{R_2,1} \\ \frac{dn_{R_2,1}}{dt} &= -k_{D,2}n_{R_2,1} \end{aligned} \quad (24)$$

These equations may be solved to give,

$$\begin{aligned} n_{R_2,1}(\Delta t) &= n_{R_2,1}(0)e^{-k_{D,2}\Delta t} + 2k_{12}\frac{(A/B)}{k_{D,2}}(1 - e^{-k_{D,2}\Delta t}) \\ &\quad - 2k_{12}\frac{(A/B)}{k_{D,2} - B}(e^{-B\Delta t} - e^{-k_{D,2}\Delta t}) \\ n_{R_2,1}(\Delta t) &= n_{R_2,1}(T_1)e^{-k_{D,2}(\Delta t - T_1)} \end{aligned} \quad (25)$$

Since we must have that  $n_{R_2,1}(T_1 + T_2) = n_{R_2,1}(0)$ , we have,

$$\begin{aligned} n_{R_2,1}(0) &= n_{R_2,1}(T_1)e^{-k_{D,2}T_2} \\ &= n_{R_2,1}(0)e^{-k_{D,2}(T_1 + T_2)} \\ &\quad + 2k_{12}\frac{(A/B)}{k_{D,2}}(e^{-k_{D,2}T_2} - e^{-k_{D,2}(T_1 + T_2)}) \\ &\quad - 2k_{12}\frac{(A/B)}{k_{D,2} - B}(e^{-BT_1 - k_{D,2}T_2} - e^{-k_{D,2}(T_1 + T_2)}) \end{aligned} \quad (26)$$

and so,

$$\begin{aligned} n_{R_2,1}(0) &= 2k_{12}\frac{A}{B}\frac{e^{-k_{D,2}T_2}}{1 - e^{-k_{D,2}(T_1 + T_2)}} \times \\ &\quad \left[\frac{1 - e^{-k_{D,2}T_1}}{k_{D,2}} - \frac{e^{-BT_1} - e^{-k_{D,2}T_1}}{k_{D,2} - B}\right] \end{aligned} \quad (27)$$

This gives,

$$\begin{aligned} n_{R_2,1}(\Delta t) &= 2k_{12}\frac{(A/B)}{k_{D,2}} \times \\ &\quad \left[1 - \left(\frac{1 - e^{-k_{D,2}T_2}}{1 - e^{-k_{D,2}(T_1 + T_2)}}\right) \right. \\ &\quad \left. - \frac{k_{D,2}}{k_{D,2} - B}\frac{1 - e^{-(BT_1 + k_{D,2}T_2)}}{1 - e^{-k_{D,2}(T_1 + T_2)}}\right]e^{-k_{D,2}\Delta t} \\ &\quad - \frac{k_{D,2}}{k_{D,2} - B}e^{-B\Delta t} \end{aligned} \quad (28)$$

Finally, the differential equation for  $n_{E_2R_2,1}$  is given by,

$$\frac{dn_{E_2R_2,1}}{dt} = 2\frac{k_{21}}{V}n_{R_2,1} - k_{22}n_{E_2R_2,1} \quad (29)$$

for  $t \in [s(T_1+T_2), s(T_1+T_2)+T_1]$ , while  $n_{E_2R_2,1}(\Delta t) = 0$  for  $t \in [s(T_1+T_2)+T_1, (s+1)(T_1+T_2)]$ .

Therefore, for  $t \in [s(T_1+T_2), s(T_1+T_2)+T_1]$ , we have,

$$\begin{aligned} n_{E_2R_2,1}(\Delta t) = & 4\frac{k_{12}k_{21}}{V}\frac{(A/B)}{k_{D,2}} \times \\ & \left[ \frac{1}{k_{22}} - \frac{1}{k_{22}}e^{-k_{22}\Delta t} \right. \\ & - \left( \frac{1 - e^{-k_{D,2}T_2}}{1 - e^{-k_{D,2}(T_1+T_2)}} - \frac{k_{D,2}}{k_{D,2} - B} \frac{1 - e^{-(BT_1+k_{D,2}T_2)}}{1 - e^{-k_{D,2}(T_1+T_2)}} \right) \frac{1}{k_{22} - k_{D,2}} e^{-k_{D,2}\Delta t} \\ & + \left( \frac{1 - e^{-k_{D,2}T_2}}{1 - e^{-k_{D,2}(T_1+T_2)}} - \frac{k_{D,2}}{k_{D,2} - B} \frac{1 - e^{-(BT_1+k_{D,2}T_2)}}{1 - e^{-k_{D,2}(T_1+T_2)}} + \frac{k_{D,2}(k_{22} - k_{D,2})}{(k_{D,2} - B)(k_{22} - B)} \right) \frac{1}{k_{22} - k_{D,2}} e^{-k_{22}\Delta t} \\ & \left. - \frac{k_{D,2}}{k_{D,2} - B} \frac{1}{k_{22} - B} e^{-B\Delta t} \right] \end{aligned} \quad (30)$$

Note then that  $n_{E_2R_2,1}$  starts at 0 and then rises to a steady-state value. Therefore, in order to maximize the average production rate of  $R_3$ , we must have that  $T_1 = \infty$ , so that the average production rate of  $R_3$  is simply given by the steady-state production rate.

When  $n_1 = n_1^+ = 2\bar{n}_1$ ,  $n_2 = n_2^+ = 2\bar{n}_2$ , the steady-state value of  $n_{E_2R_2}$  is given by,

$$n_{E_2R_2} = 4\frac{k_{12}k_{21}}{V}\frac{(A/B)}{k_{D,2}k_{22}}\bar{n}_1\bar{n}_2 \quad (31)$$

and so, when  $T_1$  is large, the total amount of  $R_3$  that is produced during the time period  $T_1$  is given by,

$$\Delta n_{R_3} = k_{22}n_{E_2R_2}T_1 = 4\frac{k_{12}k_{21}}{V}\frac{(A/B)}{k_{D,2}}\bar{n}_1\bar{n}_2T_1 \quad (32)$$

To ensure periodicity of the solution,  $T_2$  must be such that the amount of  $R_3$  consumed in the third step is equal to the amount of  $R_3$  accumulated. Assuming that the amount of  $R_3$  is infinite at all times (as with the undifferentiated case, this assumption maximizes the overall production rate of  $P$ ), then the amount of  $R_3$  consumed is given by  $2k_{32}\bar{n}_3T_2$ . We then have,

$$\frac{k_{12}k_{21}}{V}\frac{(A/B)}{k_{D,2}}(2\bar{n}_1)(2\bar{n}_2)T_1 = k_{32}(2\bar{n}_3)T_2 \quad (33)$$

Now, note that since all the enzymes are focused on either the first two tasks or the third task in the temporally differentiated model, we have  $n = 2\bar{n}_1 + 2\bar{n}_2 = 2\bar{n}_3$ . Defining  $\beta = 2\bar{n}_1/n$  therefore gives,

$$\frac{k_{12}k_{21}}{V}\frac{(A/B)}{k_{D,2}}\beta(1-\beta)n^2T_1 = k_{32}nT_2 \quad (34)$$

Note that the average production rate of  $P$  is simply given by  $k_{32}nT_2/(T_1+T_2)$ . Although  $T_1$  and  $T_2$  are both

infinite,  $T_1/(T_1+T_2)$ ,  $T_2/(T_1+T_2)$  are finite, and we can determine the optimal split between the two work cycles that maximizes the average production rate of  $P$ .

Defining  $\alpha = T_1/(T_1+T_2)$ , we get that the average production rate of  $P$  is simply  $k_{32}(1-\alpha)n$ . Diving both sides of the previous equation by  $T_1+T_2$  gives,

$$\frac{k_{12}k_{21}}{V}\frac{(A/B)}{k_{D,2}}\beta(1-\beta)\alpha n^2 = k_{32}(1-\alpha)n \quad (35)$$

As with the steady-state solution, note that we can maximize the output of  $P$  when  $\beta = 1/2$ , and so we obtain,

$$\frac{k_{12}k_{21}}{V}\frac{(A/B)}{k_{D,2}}\alpha n = 4k_{32}(1-\alpha) \quad (36)$$

Defining  $\gamma$  as before gives,

$$\alpha = \frac{1}{1+\gamma n} \Rightarrow 1-\alpha = \frac{\gamma n}{1+\gamma n} \quad (37)$$

To distinguish this  $\alpha$  from the  $\alpha$  defined in the temporally undifferentiated case, we re-denote the  $\alpha$  defined in this subsection by  $\alpha_{diff}$ .

#### IV. COMPARISON OF SYSTEM OUTPUT WITH AND WITHOUT TEMPORAL DIFFERENTIATION

We now wish to compare the rate of production of  $P$  with and without temporal differentiation, to determine whether temporal differentiation can optimize system performance. In comparing the production rate of  $P$  for both the temporally differentiated and undifferentiated cases, it makes sense to search for long-term

solutions that maximize the production of  $P$  for both cases. For, if we find that temporal differentiation outcompetes temporal non-differentiation, and if the non-differentiated case is operating at a steady-state that is not optimal, then we have not proven anything, since it is possible that a temporally non-differentiated system will produce at least as much  $P$  as a temporally differentiated system, with the appropriate steady-state solution. The converse holds if temporal non-differentiation outcompetes temporal differentiation, and temporal differentiation is not running optimally.

If we expand both the undifferentiated and differentiated expressions to second-order in  $\gamma n$ , we obtain, for small  $\gamma n$ , that,

$$1 - \alpha_{undiff} = \gamma n(1 - 2\gamma n) \quad (38)$$

for the undifferentiated case, and,

$$1 - \alpha_{diff} = \gamma n(1 - \gamma n) \quad (39)$$

so that temporal differentiation leads to a rate of production of  $P$  that is faster than the undifferentiated case. As  $\gamma n$  increases, the production advantage for temporal differentiation increases over a certain interval. Since both values of  $1 - \alpha$  approach 1 as  $\gamma n \rightarrow \infty$ , the production advantage for temporal differentiation reaches a maximum and then disappears as  $\gamma n$  grows.

Now, plugging in the explicit definitions for  $A$  and  $B$ , we obtain that,

$$\gamma n = \frac{k_{12}k_{21}/V}{4k_{32}k_{D,2}} \frac{\frac{f_R}{k_{12}}}{\frac{f_R}{k_{12}} + \frac{k_{D,1}}{(k_{11}/V)}} n \quad (40)$$

Note then that  $\gamma n$  increases with  $n$  and  $f_R$ , and decreases with  $k_{D,1}$  and  $k_{D,2}$ .

## V. DISCUSSION

### A. Justification of model parameter regimes

Our model assumes that the total number of enzymes involved in processing the resource is small, and that the intermediate  $R_3$  does not decay. The reason for the first assumption is that if the number of enzymes involved in processing the resource is large, then temporal differentiation will not lead to an increase in the production rate of  $P$ . At large enzyme numbers, the rate limiting step to the production rate is simply the input rate of external resource to the compartment.

We also assumed that  $k_{D,3} = 0$ , because we claim that a low decay rate of the intermediate  $R_3$  is a requirement for temporal differentiation to result in a higher production rate of  $P$ . Intuitively, if the decay rate of  $R_3$  is significant, then if the enzymes focus on the first two processing tasks and not on the third, the unprocessed  $R_3$  will simply decay, so that when the enzymes switch tasks and focus on processing  $R_3$ , there will be little left.

However, when the decay rate of  $R_3$  is low, then it makes sense for the enzymes to focus on the first two processing tasks for a certain time period, for during that time the rate of production of  $R_3$  is more than double what it would be without temporal differentiation. Since the  $R_3$  decays very slowly, when the enzymes switch tasks and focus on processing  $R_3$  into the final product  $P$ , little to none of the unprocessed  $R_3$  has decayed, so that almost all of the  $R_3$  produced gets converted into  $P$ .

In this paper, we assumed that  $k_{D,3} = 0$ , which means that none of the  $R_3$  decays. Therefore, optimal production rate of  $P$  is achieved with infinitely long cycle times. When  $k_{D,3}$  is positive (but still small), the decay of the unprocessed  $R_3$  means that optimal production rate of  $P$  requires a finite cycle time.

### B. The small $n$ criterion

The analytical solution of the first four differential equations governing our model explicitly made use of the assumption that  $\bar{n}_1$  and  $\bar{n}_2$  are small. We therefore need to investigate what the criteria for smallness are.

When  $n = \bar{n}_1 + \bar{n}_2 + \bar{n}_3$  is small, the rate of the first reaction is given by,

$$k_{12}n_{E_1R_1} = \frac{f_R}{\frac{f_R}{k_{12}} + \frac{k_{D,1}}{(k_{11}/V)}} \bar{n}_1 \quad (41)$$

As  $\bar{n}_1$  increases, eventually there will be enough enzyme  $E_1$  present to process all of the incoming resource. At this point, the reaction rate becomes  $f_R$ . Therefore, the transition from small  $\bar{n}_1$  to large  $\bar{n}_1$  behavior is given by the criterion [14],

$$k_{12}n_{E_1R_1} = f_R \quad (42)$$

Denoting  $\bar{n}_{1,trans}$  as the value of  $\bar{n}_1$  where the transition from small to large  $\bar{n}_1$  behavior occurs, we have,

$$\bar{n}_{1,trans} = \frac{f_R}{k_{12}} + \frac{k_{D,1}}{(k_{11}/V)} \quad (43)$$

Note that the transition point increases as  $f_R$  and  $k_{D,1}$  increase, and as  $k_{11}$  decrease.

Now, in the small  $n$  regime, the rate of the second reaction is given by,

$$k_{22}n_{E_2R_2} = \frac{(k_{21}/V)}{\frac{f_R}{k_{12}} + \frac{k_{D,1}}{(k_{11}/V)}} \bar{n}_1 \bar{n}_2 \quad (44)$$

Setting  $\bar{n}_1 = \bar{n}_2 = \bar{n}_{12}$  for maximal reaction rate, and solving the equation  $k_{22}n_{E_2R_2} = f_R$  for  $\bar{n}_{12}$ , we obtain [14],

$$\bar{n}_{12,trans} = \sqrt{\frac{k_{D,2}}{(k_{21}/V)} \left( \frac{f_R}{k_{12}} + \frac{k_{D,1}}{(k_{11}/V)} \right)} \quad (45)$$

Note that this transition point also increases as  $f_R$ ,  $k_{D,1}$  and  $k_{D,2}$  increase, and as  $k_{11}$  and  $k_{12}$  decrease. However,

note that because of the presence of the square-root, the dependence of  $n_{12,trans}$  on these various parameters is weaker than in the previous case.

In any event, the small  $n$  expressions that we developed in this paper are only valid when either  $f_R$ ,  $k_{D,1}$ , or  $k_{D,2}$  are large, or when  $k_{11}$  or  $k_{12}$  are small. This general criterion for small  $n$  makes sense: If  $f_R$  is large compared to  $n$ , then there are comparatively few agents that can handle the incoming flow of resource. If either  $k_{D,1}$  or  $k_{D,2}$  is large, then the incoming resource or intermediate decays quickly, so that there are insufficient numbers of agents that can grab and process the resource or intermediate before it decays. Finally, if either  $k_{11}$  or  $k_{12}$  is small, then the agents grab the resource or intermediate slowly, and so the resource or intermediate decays before the agents have a chance to grab and process them. In this case, too, there are insufficient numbers of agents to process all of the incoming resource.

### C. When can a temporally differentiated process outperform a non-differentiated process?

We now turn our attention to the problem of when a temporally differentiated pathway outperforms a non-differentiated pathway.

First of all, the advantage of any kind of differentiation is that, by having agents specialize in one or a few subtasks associated with a given task, they can perform this smaller set of subtasks much better than a non-specialized agent. Presumably, then, this results in faster completion of the whole task [14].

However, there is a cost to differentiation, due to the need to transport intermediates to the appropriate specialized agents. When the total number of agents is small, the transport costs are sufficiently high that the non-differentiated pathway outperforms the differentiated pathway. At higher agent numbers, however, the population density of agents becomes sufficiently high that the transport costs become sufficiently low that the differentiated pathway can outperform the non-differentiated pathway [10, 14].

The differentiated pathway can only outperform the non-differentiated pathway over a finite interval, because the production rate of the final product becomes resource limited at sufficiently high agent numbers. For these agent numbers, the differentiated and non-differentiated pathways perform similarly. Therefore, a differentiated pathway can only outperform a non-differentiated pathway when the agent-to-resource ratio is at intermediate values. Furthermore, the greater the flow rate of resource, the greater the likelihood that the differentiated pathway will outperform the non-differentiated pathway. The reason for this is that, as the flow rate of resource grows, the agent number at which the production rate of  $P$  becomes resource limited is pushed to higher agent numbers, and so the interval over which the differentiated pathway outperforms the non-differentiated pathway is

longer.

Thus far, our discussion has only focused on the non-temporal division of labor. With temporal division of labor, the agents do not specialize in only one or a few subtasks, but rather oscillate between the various subtasks of the overall process. In principle, given enough time, a given agent can “learn” the given subtask and optimize its performance to equal that of the specialized agent. If this optimization time is negligible, then under certain conditions (such as those in our model), the temporally differentiated process will outperform the non-temporally differentiated process.

If the optimization time is positive, a temporally differentiated process can outperform a non-temporally differentiated process if the decay rate of the intermediate  $R_3$  is 0. The reason for this is that, for the temporally differentiated process, the optimal production rate of  $P$  is achieved with an infinite cycle time. Therefore, the finite optimization time has a negligible effect on the overall production rate.

However, if  $k_{D,3} > 0$ , then the temporally differentiated pathway will only perform optimally with a finite cycle time. For if the time period during which the agents focus on the first two subtasks is infinite, then the accumulated  $R_3$  will decay away, resulting in a low production rate of  $P$ . In this case, the optimization time will have an effect on the overall production rate. Here, in order for the temporally differentiated pathway to outperform the non-temporally differentiated pathway, the production rate of the temporally differentiated pathway with a zero optimization time must be sufficiently greater than the production rate of the non-temporally differentiated pathway, so that the reduction in production rate due to a positive optimization time does not erase the superior performance of the temporally differentiated pathway.

Now, when  $n$  is sufficiently small, we have already explained that a non-differentiated process will outperform a differentiated one. For larger  $n$ ,  $n$  may still be sufficiently small that the low-order expansions used in this paper are valid, but large enough that the differentiated pathway can overtake the non-differentiated pathway.

If  $n$  is in either of these regimes, then at low values of  $f_R$ , the value of  $\gamma n$  may be sufficiently small that the cost associated with temporal differentiation means that it is not an optimal labor strategy (as measured by comparing the values of  $1 - \alpha_{undiff}$  and  $1 - \alpha_{diff}$ ).

At higher values of  $f_R$ , the value of  $\gamma n$  can rise to a level where the temporally differentiated pathway with a negligible optimization time is significantly more efficient than the non-differentiated strategy. Therefore, even with a cost arising from a positive optimization time, the temporally differentiated strategy outperforms the non-temporally differentiated strategy.

Thus, in the small  $n$  regime, increasing the value of  $f_R$  at a given value of  $n$  increases the performance advantage of the temporally differentiated labor strategy.



## D. Implications for sleep

In the context of sleep, the implications of the results presented here are that sleep emerges because the brain can process more tasks if it adopts a temporally differentiated labor strategy. Presumably, the more tasks a brain can accomplish within a given amount of time, the greater the survival advantage for the organism, providing an evolutionary selection pressure for temporally differentiated labor strategies.

In our model, we have seen that an optimal ratio between the times devoted to two different sets of process subtasks emerges, even with a constant inflow of external resource. In the context of sleep, this suggests a natural sleep cycle that can exist independently of any external day-night regulation. This also suggests an evolutionary basis for sleep that could apply to nocturnal organisms [27].

This being said, the presence of a day-night cycle could nevertheless regulate the exact location of the various subtask time intervals. Presumably, it makes sense for most organisms to remain alert during the day, when external information is most available, and to process that information at night, when external information is less available (the ability to avoid predators and to hunt stealthily are probably the major selection pressures driving the emergence of nocturnal organisms) [24].

As described in the Introduction, we also argue that the model presented in this paper suggests an evolutionary basis for the emergence of distinct REM and non-REM sleep states from an earlier undifferentiated sleep state. As the brain complexity increases, and the amount of information that must be processed during the sleep state increases, it becomes more efficient for the brain to oscillate between various information processing and consolidation subtasks associated with the sleep state itself [24, 26].

## VI. CONCLUSIONS AND FUTURE RESEARCH

This paper presented a highly simplified three-step model for the conversion of some external resource into a final product. We showed that, when the number of agents available for processing the resource is small, and when the second intermediate does not decay, then the production rate of the final product can be maximized if the agents oscillate between the first two subtasks and the third subtask. Based on these results, we conjectured that sleep and the emergence of REM and non-REM sleep

are driven by a selective advantage for a temporally differentiated labor strategy.

Because our model assumed that the second intermediate does not decay, we obtained an optimal cycle time that was infinite, though the ratio of times allocated to the various sets of subtasks during a given cycle was well-defined. For future research, we would like to explore how the optimal cycle time is affected when we assume a small, but positive value for  $k_{D,3}$ . Presumably, this will lead to an optimal cycle time that is finite, for if the cycle time is infinite, then when the agents switch to the third task, all of the accumulated  $R_3$  will have decayed away, so that the production rate of  $P$  will be 0.

In the context of biological systems, it is known that sleep oscillates between REM and non-REM states with a well-defined cycle time. It would be interesting to develop a model along the lines of the model considered in this paper that, based on a few experimentally measurable parameters, could predict the REM/non-REM cycle times via an optimization criterion. Along these lines, it would be interesting to also develop a model that could similarly predict the sleep/wake cycles of animals that have little to no exposure to the sun, such as rats (so that their sleep/wake cycles must be internally regulated) [27].

We explained in the previous section that a finite cycle time, combined with an optimization time for enzyme efficiency, can lead to distinct parameter regimes where temporal differentiation either outperforms or underperforms non-temporal differentiation. The characterization of these specific parameter regimes is an issue that we plan to explore in future work as well.

Finally, in this paper we considered a fundamentally non-linear model. This was necessary, since a linear dependence of process rates on agent number will not give an advantage to temporal differentiation with a mean-field description of the dynamics. However, when agent numbers are small, stochastic effects can become important, since it is impossible to have fractional agents, and since it is often not possible to split tasks (i.e. either a task is completed or it is not). In this situation, even a fundamentally linear system can optimize its output via a temporally differentiated labor strategy. The influence of stochastic effects on temporal differentiation is an issue that will also be explored in future work.

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